

Application No. 10/646,070  
Amendment dated February 28, 2007  
Reply to Office Action of August 28, 2006

Docket No.: 025122.0101N1US

# REMARKS

# BEST AVAILABLE COPY

The Office Action dated August 28, 2006 has been reviewed and the comments of the U.S. Patent and Trademark Office have been considered. The following remarks are respectfully submitted to place the application in condition for allowance.

A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier. Claims 1-47 were previously canceled. Claims 49-106 are presently canceled. Claim 48 is currently amended. New claims 107-145 are being added to the application. Support for the amendment may be found, for example, at least in the following sections of the original disclosure: page 6, lines 21-30; page 7, lines 11-19; page 8, lines 8-13, 21, and 18-30; page 9, lines 5-30; page 10, lines 1-11; page 15, lines 4-28; page 16, lines 26-30; page 17, lines 5-7; page 18, lines 3-11 and 15-22; page 19, lines 21 and 24-29; page 20, lines 4 and 29; page 21, lines 18-28; page 22, lines 3, 7 and 20-30; page 23, lines 1-20; page 24, lines 23-24; page 25, lines 19-30; page 26, lines 1-3 and 29; page 27, lines 7-9 and 23-29; page 29, lines 23-29; page 30, lines 5 and 20-23; page 31, lines 24-30; page 33, lines 12-29; page 35, lines 16-18; page 36, lines 21-24 and page 30; page 38, lines 16 and 21 through page 40, line 1; page 50, lines 11-13.

## Priority

The Examiner found that Applicant did not comply with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120, specifically the disclosure of the prior-filed applications, Application No. 09/100,812 and Application No. 09/646,807, fail to provide adequate support or enablement in the manner provided by the 35 U.S.C. 112, first paragraph, for claims 48-91. Applicant respectfully disagrees that the priority applications do not provide support for the claims. To further prosecution of this application, however, Applicant

Application No. 10/646,070  
Amendment dated February 28, 2007  
Reply to Office Action of August 28, 2006

Docket No.: 025122.0101N1US

has canceled claims 49-106. Applicant has amended claim 48 in the present amendment, and provided support for each element of the claim as delineated above.

#### Oath/Declaration

The Examiner found the oath or declaration defective under 37 CFR 1.67(a) because Claim 77 contained new matter not in the parent applications and requires a new oath or declaration be filed for this application. Applicant has canceled Claim 77 in the present amendment, therefore, an issue of new matter invalidating the oath or declaration is moot. Applicant respectfully requests withdrawal of the requirement to submit a new oath or declaration.

#### Information Disclosure Statement

The Examiner considered the international and European search reports and examination reports but did not initial them because they are not considered published documents. Applicant appreciates the Examiner's consideration of the reports. Applicant listed the reports on the form PTO-1449 separately from any references cited in the reports merely as the source of references cited therein.

The Examiner acknowledged the two exhibits Applicant submitted in the Information Disclosure Statement submitted February 11, 2005, which contain the references relating to the pending litigation of patent 6,573,099, and placed the exhibits in the file. The Examiner has not considered the references because they are not listed on PTO form 1449. Exhibits A and B list references submitted by an adverse party during litigation of the '099 patent. Applicant submitted the lists in the present application to comply with the ethical duty to disclose known information to the US Patent and Trademark Office. Applicant points out that the lists contain the full and complete set of material made known to the Applicant as submitted by the adverse party in the litigation.

Application No. 10/646,070  
Amendment dated February 28, 2007  
Reply to Office Action of August 28, 2006

Docket No.: 025122.0101N1US

### Specification

The Examiner noted that part of the abstract of the disclosure provided was cut off, making it unreadable. Applicant is submitting an amendment to the abstract in the present amendment. Applicant respectfully requests entry of the amended abstract.

### Claim Objection

The Examiner objected to Claims 72-75 and 82-92 because of improper form for a dependent claim, specifically "A(a)n isolated gene construct according to claim." The Examiner suggested replacing "A(a)" with "T(t)" in the claims. Applicant appreciates the Examiner's suggestion. Applicant, however, has canceled Claims 72-75 and 82-82, which renders the edit moot. Applicant respectfully requests withdrawal of the objection.

### Claim Rejections Under 35 USC § 112

The Examiner rejected claims 48-91 under 35 USC § 112, first paragraph, for failing to comply with the written description requirement. Office Action at 7-10. The Examiner asserted that claims 48-91 filed as new claims on 8/22/03 and amended on 12/15/04 and 4/7/05 were filed without support and there did not appear to be a written description of the new claims in the application as filed. Applicant respectfully disagrees that the application does not provide a written description of the claims. To expedite prosecution of the present application, however, Applicant has canceled claims 49-91, thus rendering the rejection with respect to those claims moot.

Applicant has amended claim 48 to recite a synthetic gene which is capable of reducing the expression of a target gene in a human cell which is transfected or transformed with the synthetic gene comprising a structural gene region which comprises multiple copies of a nucleotide sequence of greater than 20 consecutive nucleotides which is identical to the sequence of the target gene or a region thereof, and wherein multiple copies of the nucleotide sequence are

Application No. 10/646,070  
Amendment dated February 28, 2007  
Reply to Office Action of August 28, 2006

Docket No.: 025122.0101N1US

arranged in an interrupted palindrome sequence and placed operably under the control of a single promoter sequence which is operable in the human cell. Support for claim 48 as amended may be found in the original disclosure and the priority documents, as indicated above. In light of the amendment to claim 48, the claim is compliant with the requirements of 35 U.S.C. §112, first paragraph, and Applicant requests withdrawal of the rejection of the claim.

The Examiner rejected claim 54 under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that applicant regards as the invention. Office Action at 10. The Examiner asserted that the phrase "is above about 10 and below about 50 nucleic acid in length" is relative and indefinite. Applicant has canceled claim 54 in the present amendment, rendering the rejection moot. Applicant, therefore, requests withdrawal of the rejection of the claim.

#### Claim Rejections under 35 USC 102

The Examiner rejected claims 48, 50, 58, 60, 62, 64, 68, 70, 72, 74, 78, 80, 82, 84, 88 and 90 under 35 U.S.C. 102(e) as being anticipated by Fire *et al.* (US 6,506,559, cited on a PTO-1449). Office Action at page 11. The Examiner specifically asserted that Fire *et al.* teach a vector comprising a construct comprising a promoter operably linked to a nucleotide sequence comprising a sense strand and an antisense strand of the target gene. Related to dependent claims, the Examiner asserts Fire *et al.* teach the promoter can be a T7 and T3 promoters, the nucleotide sequence may be at least 25 or 50 bases, the vector can be introduced into a cancerous cell, including cancer cells found in humans, a viral vector can be used as the vector, the cell can comprise a target gene at risk from a pathogen including HIV, the target gene can be an endogenous from in a human cell, the structural gene can comprise one or more strands of the nucleotide sequence, and the vector can be in combination with a carrier.

Application No. 10/646,070  
Amendment dated February 28, 2007  
Reply to Office Action of August 28, 2006

Docket No.: 025122.0101N1US

Applicant respectfully disagrees with the rejection. To further prosecution of this application, however, Applicant has cancelled claims 50, 58, 60, 62, 64, 68, 70, 72, 74, 78, 80, 82, 84, 88 and 90, thus making the rejection related to those claims moot. Applicant has amended claim 48 to recite a synthetic gene which is capable of reducing the expression of a target gene in a human cell which is transfected or transformed with the synthetic gene. The synthetic gene comprises a structural gene region which comprises multiple copies of a nucleotide sequence of greater than 20 consecutive nucleotides which is identical to the sequence of the target gene or a region thereof. The copies of the nucleotide sequence are arranged in the structural gene region in an interrupted palindrome sequence and placed operably under the control of a single promoter sequence which is operable in the human cell. Fire *et al.* do not teach these elements or this arrangement or combination of elements as presently claimed.

Specifically, Fire *et al.* do not teach a synthetic gene. Fire *et al.* also do not teach multiple copies of a nucleotide sequence. Fire *et al.* discloses the nucleotide sequence may be at least 25, 50 or 100 nucleotides. They do not have a minimum length of greater than 20 consecutive nucleotides. Fire, *et al.* do not teach copies of a nucleotide sequence arranged as an interrupted palindrome sequence. Fire *et al.* also do not teach a nucleotide sequence placed operably under the control of a single promoter. Clearly, Fire *et al.* do not teach each and every element of claim 48 or the arrangement of those elements as recited in the claim. The newly added claims incorporate all of the limitations of amended claim 48. Fire *et al.*, therefore, do not anticipate the presently claimed invention. Applicant respectfully requests withdrawal of the rejection of anticipation at to Fire *et al.*

The Examiner further rejected claims 48-52, 55, 58, 62-63, 72-73 and 86-91 under 35 U.S.C. §102(b) as being anticipated by Dorer *et al.* (*Cell*, 77:993-1002 (1994)). Office Action at 12. The Examiner alleged that Dorer *et al.* teach a synthetic gene comprising a dispersed nucleic

Application No. 10/646,070  
Amendment dated February 28, 2007  
Reply to Office Action of August 28, 2006

Docket No.: 025122.0101N1US

acid molecule comprising tandem copies of a nucleic acid sequence which is substantially identical to the nucleic acid molecule of the mini-white target gene placed operably under control of a promoter sequence. The Examiner contended that the synthetic gene taught by Dorer *et al* meets all of the limitations of claims 48-52. The Examiner also contended that Dorer *et al* further teach a synthetic gene comprising tandem inverted and/or direct repeats of a genetic sequence that is endogenous to the genome of an animal (i.e., *Drosophila*) cell and tandem copies of the nucleotide sequence operably linked to spatially separate promoter sequences.

Applicant respectfully disagrees with the rejection. To further prosecution of this application, however, Applicant has cancelled claims 49-52, 55, 58, 62-63, 72-73 and 86-91 are canceled, thus making the rejection with respect to these claims moot. Claim 48 as amended recites a synthetic gene which is capable of reducing the expression of a target gene in a human cell. The synthetic gene comprises a structural gene region comprising multiple copies of a nucleotide sequence of greater than 20 consecutive nucleotides. The structural gene sequence is identical to the sequence of the target gene or a region thereof. Multiple copies of the nucleotide sequence are arranged in the structural gene region in an interrupted palindrome sequence, which are placed operably under the control of a single promoter sequence which is operable in the human cell. Dorer *et al* do not teach all of the elements of the presently claimed invention.

Specifically, Dorer *et al* do not teach a synthetic gene operable in a human cell. They do not disclose the feature of the minimum length of greater than 20 consecutive nucleotides identical to the sequence of the target gene or a region of the target gene. They do not teach the nucleotide sequences arranged as an interrupted palindrome. In addition, Dorer *et al* do not teach multiple copies of a nucleotide sequence arranged in an interrupted palindrome sequence and placed operably under the control of a single promoter sequence operable in a human cell. Dorer *et al* do not teach each and every element or the arrangement of those elements as recited

Application No. 10/646,070  
Amendment dated February 28, 2007  
Reply to Office Action of August 28, 2006

Docket No.: 025122.0101N1US

in claim 48. The newly added claims incorporate all of the limitations of amended claim 48. Dorer *et al.*, therefore, do not anticipate the present invention. Applicant, therefore, respectfully requests withdrawal of the rejection.

#### Claim Rejections under 35 USC 103

The Examiner rejected claims 49, 51, 52, 55, 56, 57, 59, 61, 63, 66, 69, 71, 75, 79, 81, 83, 85 and 87-91 under 35 USC 103(a) as being unpatentable over Fire *et al.*, U.S. Patent No. 6,506,559 taken with Conrad, U.S. Patent No. 6,054,299. The Examiner further rejected claims 55 and 71 under 35 USC 103(a) as being unpatentable over Fire *et al.* (U.S. Patent No. 6,506,559) taken with Conrad (U.S. Patent No. 6,054,299) and further in view of Wang *et al.* (U.S. patent application no. 20020150968). Applicant respectfully disagrees that the claims are obvious over the cited references. Applicant has cancelled claims 49-91, however, thus making the rejection with respect to these claims moot.

The Examiner rejected claim 48 under 35 USC 103(a) as being unpatentable over Fire *et al.*, U.S. Patent No. 6,506,559 taken with Ladner *et al.*, U.S. Patent No. 5,198,346, and Fire *et al.*, U.S. Patent No. 6,506,559, taken with D'Apice.

In levying an obviousness rejection under 35 U.S.C. §103, the Examiner has the burden of establishing that at the time of the invention, there was: (1) some suggestion or motivation to modify the reference or to combine reference teachings, (2) a reasonable expectation of success, and (3) that the prior art references, when combined, taught or suggested all the claim limitations. See MPEP §2143 (Aug. 2001, Latest Revision August 2006); *See also In re Royka*, 490 F.2d 981, 985 (C.C.P.A. 1974). Obviousness may not be established based upon hindsight or the teachings or suggestions of the inventor. *W. L. Gore & Assoc., Inc. v Garlock, Inc.*, 721 F.2d 1540, 1551-1553 (Fed. Cir. 1983); *Ruiz v A. B. Chance Co.*, 357 F.3d 1270, 1276 (Fed. Cir. 2004).

Application No. 10/646,070  
Amendment dated February 28, 2007  
Reply to Office Action of August 28, 2006

Docket No.: 025122.0101N1US

Here, this burden has not been met. It is respectfully submitted that the obviousness rejection to claim 48 fails on each of the three grounds as detailed below.

Applicant has amended claim 48 to recite a synthetic gene which is capable of reducing the expression of a target gene in a human cell which is transfected or transformed with the synthetic gene. The synthetic gene comprises a structural gene region which comprises multiple copies of a nucleotide sequence of greater than 20 consecutive nucleotides identical to the sequence of the target gene or a region thereof. Multiple copies of the nucleotide sequence are arranged in the structural gene region in an interrupted palindrome sequence and placed operably under the control of a single promoter sequence which is operable in the human cell.

As previously noted, Fire *et al.* do not teach nor contemplate a synthetic gene. Fire *et al.* also do not teach multiple copies of a nucleotide sequence, or a minimum length of greater than 20 consecutive nucleotides. They do not teach an interrupted palindrome sequence. Fire *et al.* do not teach or suggest multiple copies of the nucleotide sequence are arranged in the structural gene region in an interrupted palindrome sequence and placed operably under the control of a single promoter sequence which is operable in the human cell. Fire *et al.* do not teach or suggest each and every element of claim 48 or the arrangement of those elements as recited in the claim.

The deficiencies of Fire *et al.* are not overcome by addition of the secondary references. Neither Ladner *et al.* nor D'Apice *et al.* teach a synthetic gene. They do not teach or suggest any of the other elements of the invention. In addition, one of skill would not be motivated to mix and match the disparate parts of Fire *et al.* with the entirely different form of gene repression found in Ladner *et al.* and D'Apice *et al.* to address iRNA.

As shown, Fire *et al.* do not teach each and every element of the presently claimed invention. This deficiency is not cured by combination with the secondary references where the



Application No. 10/646,070  
Amendment dated February 28, 2007  
Reply to Office Action of August 28, 2006

Docket No.: 025122.0101N1US

combination does not teach each and every element of the presently claimed invention.

Applicant respectfully requests withdrawal of the rejection.

#### Double Patenting

The Examiner states that claims 48-75 and 78-97 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 34-43, 53-63, and 65 of copending Application no. 10/346,853. In the present application, Applicant has canceled claims 49-106. Claim 48 is amended and claims 107-145 added in the present application. Applicant submits that the amendment eliminates any consideration of double patenting issues with Application No. 10/346,853. Applicant respectfully requests withdrawal of the rejection. In the event the Examiner further finds obviousness-type double patenting in the application, Applicant will address such rejection upon indication of allowable subject matter.

#### Conclusion

In view of the above amendment, Applicant believes the pending application is in condition for allowance and requests favorable action on the merits. Should the Examiner feel that any issues remain, Applicant requests that the Examiner contact the undersigned so that the issues may be expeditiously addressed and prosecution of the instant application continue.

Applicants submit concurrently a request for extension of time under 37 C.F.R. 1.136 and the accompanying fee. In the event that any additional extensions of time are necessary to prevent the abandonment of this patent application, then such extension of time are hereby petitioned. The U.S. Patent and Trademark Office is hereby authorized to charge any fees that may be required in conjunction with this submission to Deposit Account Number 50-2228, referencing matter number 025122.0101N1US (previously 023004.0104N1US) from which the undersigned is authorized to draw.

Dated: February 28, 2007

Respectfully submitted,

18

3671645

Application No. 10/646,070  
Amendment dated February 28, 2007  
Reply to Office Action of August 28, 2006

Docket No.: 025122.0101N1US

By 

Therese M. Finan

Registration No.: 42,533

PATTON BOGGS LLP

8484 Westpark Drive, 9th Floor

McLean, Virginia 22102

(703) 744-8069

(703) 744-8001 (Fax)

Attorney for Applicants

**This Page is Inserted by IFW Indexing and Scanning  
Operations and is not part of the Official Record**

**BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

- ☐ **BLACK BORDERS**
- ☐ **IMAGE CUT OFF AT TOP, BOTTOM OR SIDES**
- ☐ **FADED TEXT OR DRAWING**
- ☐ **BLURRED OR ILLEGIBLE TEXT OR DRAWING**
- ☐ **SKEWED/SLANTED IMAGES**
- ☐ **COLOR OR BLACK AND WHITE PHOTOGRAPHS**
- ☐ **GRAY SCALE DOCUMENTS**
- ☒ **LINES OR MARKS ON ORIGINAL DOCUMENT**
- ☐ **REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY**
- ☐ **OTHER:** \_\_\_\_\_

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.**